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**Fezf2 expression identifies a multipotent progenitor for neocortical projection neurons, astrocytes, and oligodendrocytes.**

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**Public Summary:**

Progenitor cells in the cerebral cortex sequentially generate distinct classes of projection neurons. Recent work suggests the cortex may contain intrinsically fate-restricted progenitors marked by expression of Cux2. However, the heterogeneity of the neocortical ventricular zone as well as the contribution of lineage-restricted progenitors to the overall cortical neurogenic program remains unclear. Here, we utilize in vivo genetic fate mapping to demonstrate that Fezf2-expressing radial glial cells (RGCs) exist throughout cortical development and sequentially generate all major projection neuron subtypes and glia. Moreover, we show that the vast majority of CUX2(+) cells in the VZ and SVZ are migrating interneurons derived from the subcortical telencephalon. Examination of the embryonic cortical progenitor population demonstrates that Cux2(+) RGCs generate both deep- and upper-layer projection neurons. These results identify Fezf2(+) radial glial cells as a multipotent neocortical progenitor and suggest that the existence, and molecular identity, of laminar-fate-restricted RGCs awaits further investigation.

**Scientific Abstract:**

Progenitor cells in the cerebral cortex sequentially generate distinct classes of projection neurons. Recent work suggests the cortex may contain intrinsically fate-restricted progenitors marked by expression of Cux2. However, the heterogeneity of the neocortical ventricular zone as well as the contribution of lineage-restricted progenitors to the overall cortical neurogenic program remains unclear. Here, we utilize in vivo genetic fate mapping to demonstrate that Fezf2-expressing radial glial cells (RGCs) exist throughout cortical development and sequentially generate all major projection neuron subtypes and glia. Moreover, we show that the vast majority of CUX2(+) cells in the VZ and SVZ are migrating interneurons derived from the subcortical telencephalon. Examination of the embryonic cortical progenitor population demonstrates that Cux2(+) RGCs generate both deep- and upper-layer projection neurons. These results identify Fezf2(+) radial glial cells as a multipotent neocortical progenitor and suggest that the existence, and molecular identity, of laminar-fate-restricted RGCs awaits further investigation.

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